

ABSTRACT

"Black holes" in the genomes of bacterial pathogens represent deletions of "anti-virulence" genes, i.e. genes that are detrimental to a pathogenic lifestyle. Identification of the missing genetic loci in the "black hole" identifies genes that are incompatible with the bacteria's pathogenicity. These
5 genes, their gene products, and compounds generated by the enzymatic action of these gene products represent potential new compounds that are inhibitory to the bacterial pathogen and thus useful as pharmaceuticals. The utility of this concept is demonstrated in the missing gene for lysine decarboxylase, and the resulting inhibitory activity of cadaverine (the diaminoalkyl reaction product of lysine decarboxylase) on the *Shigella* enterotoxins. Diaminoalkyl compounds are therefore potent
10 inhibitors of *E. coli* and *Shigella* spp. enterotoxins. Lysine decarboxylase generated from the gene *cadA* results in attenuation of the enterotoxic effects. New methods of use of diaminoalkyl compounds as medicaments are described. New uses of genetic constructs containing a *cadA* sequence, or other "anti-virulence" gene, for biochemical probes, for toxin receptor identification, and for pharmaceutical discovery are described. Additional uses are described for vaccines and DNA vaccine delivery.